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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/382,794	08/25/1999	ANATOLY DRITSCHILO	010091-041	5682

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EXAMINER	
FISHER, ABIGAIL L	
ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/382,794	DRITSCHILO ET AL.	
	Examiner	Art Unit	
	ABIGAIL FISHER	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-37, 39, 41, 43-44 and 71-73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-37,39,41,43,44 and 71-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 18 2009 has been entered.

Receipt of Amendments/Remarks filed on September 18 2009 is acknowledged. Claims 1-33, 38, 40, 42 and 45-70 were/stand cancelled. Claim 34 was amended. Claims **34-37, 39, 41, 43-44 and 71-73** are pending.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 34-37, 39, 41, 43-44, and 72 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is **withdrawn** in light of Applicants' amendments filed on September 18 2009.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 34-37, 39, 41, 43-44, and 71-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rashid (GB 2243777, PTO Form 1449) in view of Sioshansi et al. (US Patent No. 6030333).

Applicant Claims

Applicant claims a device consisting of a hollow seed and a therapeutic agent comprising a radionuclide and a nucleic acid sequence or a protein or polypeptide.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Rashid is directed to a device for implantation comprising a chamber containing an active ingredient which is released through a capillary bore (abstract). The device is constructed from a **cylindrical** tube containing the active ingredient (page 2, last two sentences). The length of the device is from 5 to 100 mm (0.2 to 3.9 in) with an external diameter of 1 to 40 mm (0.04 to 1.6 in) (page 3, 1-4). The internal diameter is from 0.1 to 10 mm (0.004 to 0.4 in) (page 4, line 7-8). If required, the open end of the capillary tube may be provided with a copy which dissolves away on administration, for example formed from a sugar or gelatin (page 5, second paragraph). Figure 1 indicates that each end is sealed with a water soluble sugar end cap (page 9, Fig 1 description). It is disclosed that the device can be formed of a plastics material, a ceramic material, a metal such as stainless steel, or glass. (page 3, lines 4-6). Suitable ceramic materials include **titanium** or its alloys (page 3 line 22). It is disclosed the invention is intended

for subcutaneous implantation, insertion into body cavities and may also be used for oral administration (page 5, second paragraph). The active ingredient may be a medicament, a contraceptive, or for prophylactic, diagnostic or nutritional use (page 5, last paragraph). Various different actives are listed (page 6-7).

Ascertainment of the Difference Between Scope the Prior Art and the Claims *(MPEP §2141.012)*

Rashid does not specify that the active agents are a radionuclide and a nucleic acid sequence, protein, or polypeptide. However, this deficiency is cured by Sioshansi et al.

Sioshansi et al. is directed to implantable radiotherapy device. It is disclosed that for radiation therapy that a patient is exposed from an external beam or that the radioactivity may be incorporated into an implantable device (column 1, lines 36-40). Seeds which are utilized to implant the radioactivity are implanted individually at a treatment site within and/or around a lesion (column 1, line lines 61-65). These seeds when as radiotherapy devices are discrete, or point, sources of radiation (column 1, lines 67). It is disclosed that in order to deliver both radiation and non-radiation treatments together it may be desirable to apply one more non-radioactive therapeutic agents. Therapeutic agents for example biological agents such as proteins and growth factors can be included (column 11, lines 56-63). The radiation therapy includes radionuclides such as ^{45}Ca, ^{123}Sn, ^{89}Sr, ^{32}P, ^{33}P, ^{103}Pd, and ^{123}I (column 12, lines 57-61).

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art to combine the teachings of Rashid and Sioshansi et al. and utilize a radionuclide and a protein as the active agent. One of ordinary skill in the art would have been motivated to utilize a radionuclide and a protein because it is taught in the art that this type of combination is useful in various therapies as taught by Sioshansi et al. Further more, the selection of a specify drug is considered prima facie obvious depending on the desired condition/symptoms to be treated.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Regarding the limitation of the seed having openings at each end, the ends of the invention of Rashid are open. During the formation they may be capped, if required. However, even if they are capped, once they are implanted, the cap dissolves therefore at that point the cap no longer exists and the opening are completely open.

Regarding the claimed dimensions of the seed, in the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. **See MPEP 2144.05 [R-5]**

Response to Arguments

It is noted that the arguments made after-final are substantially the same as those made after the non-final rejection. The examiner reiterates why those arguments are not considered persuasive.

Applicants argue that (1) the Office action fails to acknowledge that applicants' independent claims 34 and 71 recite a drug delivery device consisting of only the recited elements which follow and therefore the recitation of a capillary bore recited by Rashid is excluded. Applicants argue that (2) in Office action indicates that Sioshansi is directed to implantable seeds however, Sioshansi as argued by applicants is not directed to implantable seeds but devices for rendering seeds obsolete. Applicants argue that Sioshansi is not for the controlled diffusion of the therapeutic agent which comprises the claimed combination of therapeutic agents. Applicants' argue that (3) the cited prior art does not teach controlled delivery of the active.

Applicants' arguments filed December 1 2008 have been fully considered but they are not persuasive.

Regarding applicants' first argument, the examiner acknowledges applicants' claim language of consisting of. However, the claims as currently written state that "a drug delivery device consisting of a hollow seed...said hollow seed **containing**...". Therefore, the drug delivery device can consist only of a hollow seed however, the claim langue of containing which is synonymous with comprising (**Note: MPEP 2111.02)** would allow for other things to be present in or coated on the hollow seed. The claims as currently written with the claim language of containing would allow for anything to be

present inside the hollow seed. Therefore, the bore of Rashid, which is present inside the hollow seed, is not excluded by the instant claim language.

Regarding applicants' second argument, the examiner did not state that Sioshansi is directed to implantable seeds. The examiner indicated that Sioshansi is directed to an implantable device and that seeds are taught as one device utilized to implant radioactivity. The difference between the instant invention and that of Rashid is that Rashid does not explicitly teach the same claimed combination of active ingredients. However, Rashid do teach that the device can be utilized to deliver active ingredients. Shoshoni is relied upon to show that for radiotherapy treatment implantable therapeutic agents that are useful include a combination of both radiation and non-radiation treatments. Non-radiation treatments taught include proteins and radiation treatments include radionucleotides. Therefore, it would have been obvious to one of ordinary skill in the art to utilize the non-radiation and radiation treatments taught by Sioshansi in the delivery device of Rashid when desiring a device for radiotherapy.

Regarding applicants' third argument, Rashid is directed to a sustained release device as evidenced by the title and disclosure. A sustained release device encompasses controlled release.

Therefore, the rejection is maintained since applicant has not provided any persuasive arguments to overcome the rejection.

Claims 34-37, 39, 41, 43-44, and 71-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee (US Patent No. 5629008) in view of Sioshansi et al..

Applicant Claims

Applicant claims a device consisting of a hollow seed and a therapeutic agent comprising a radionuclide and a nucleic acid sequence or a protein or polypeptide.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Lee is directed to a method and device for long-term delivery of drugs. It is taught that it is often advantageous to be able to deliver a drug directly to the site which needs to be treated and thereby avoid systemic administration of the drug. This is especially true where the drug may be harmful to certain other tissues or organs if administered systemically. Localized delivery allows one to deliver high concentrations of the desired drug to a specific region of the body and yet not harm other tissues and organs (column 1, lines 58-65). The invention is a device for delivery of a therapeutic agent to a tissue or organ. The device comprises a container with a biodegradable matrix therein. The biodegradable matrix is admixed with a therapeutic agent. The container can be implanted into a tissue and will deliver a therapeutic agent (column 3, lines 1-7). Preferably, the container is a cylinder with at least one opening to the tissue in which the cylinder is implanted. The cylinder can be manufactured from material such as stainless steel, titanium or other types of medical/surgical grade plastics or metals (column 3, lines 21-25). Examples of organs include stomach, intestines, bladder, esophagus, and prostate (column 4, lines 21-28 and example XIII). Example XIII

indicates that the device is inserted into the patient's prostate or bladder. It is taught that as shown in Fig. 1, the ends of the cylinder are preferably open to the tissue (column 5, lines 29-30). The length of the cylinder is 0.1 to 3 cm (0.04 to 1.18 inches) and a diameter of 0.1 to 3 cm (0.04 to 1.18 inches). Another shape is a ring which has a outer diameter of 1.2 mm (0.05 in) and an inner diameter of 200 microns (0.2 mm and 0.008 inches) (column 5, lines 40-64). Biodegradable matrix material includes polypeptides, nucleic acids, collagen, polyamino acids, amino acids, etc. (columns 5-6, lines 65-67 and 1-11). Specific active agents taught include agents such as antineoplastic agents (anti-cancer) (column 6, lines 12-21).

Ascertainment of the Difference Between Scope the Prior Art and the Claims *(MPEP §2141.012)*

While Lee teaches that the device is utilized for site specific delivery of therapeutic agents, Lee does not explicitly state inserting within about 1 mm of said targeted site. While Lee teaches specifics regarding the length and diameter of the preferred cylindrical shape, Lee does not explicitly teach the thickness or hole diameter.

Lee does not specify that the active agent is a radionuclide or teach utilizing a matrix made from amino acids or nucleic acids in combination with radionuclides. However, this deficiency is cured by Sioshansi et al.

Sioshansi et al. is directed to implantable radiotherapy device. It is disclosed that for radiation therapy that a patient is exposed from an external beam or that the radioactivity may be incorporated into an implantable device (column 1, lines 36-40). Seeds which are utilized to implant the radioactivity are implanted individually at a treatment site within and/or around a lesion (column 1, line lines 61-65). These seeds

when as radiotherapy devices are discrete, or point, sources of radiation (column 1, lines 67). It is disclosed that in order to deliver both radiation and non-radiation treatments together it may be desirable to apply one more non-radioactive therapeutic agents. Therapeutic agents include chemical agents, proteins and growth factors (column 11, lines 56-63). The radiation therapy includes radionuclides such as ^{45}Ca, ^{123}Sn, ^{89}Sr, ^{32}P, ^{33}P, ^{103}Pd, and ^{123}I (column 12, lines 57-61).

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to utilize the drug delivery device of Lee in a method of delivering a therapeutic agent and inserting the therapeutic containing container within about 1 millimeter of the target site. One of ordinary skill in the art would have been motivated to insert the delivery device as close to the target site as possible as Lee teaches that the device is utilized for site specific delivery of a therapeutic agent and that it is often advantageous to be able to deliver a drug directly to the site which needs to be treated and thereby avoid systemic administration of the drug. Furthermore, Lee specifically teaches inserting the device into the desired tissue/organ, therefore a reasonable interpretation of this teaching is that the delivery device is inserted at the target site, which would be within 1 mm of the site.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Lee and Sioshansi et al. and utilize the drug delivery device of Lee to deliver an anti-neoplastic agent and radionuclides. One of ordinary skill in the art would have been motivated to cancer as Lee teaches insertion

into the prostate and teaches that the drug of choice can be an anti-neoplastic (anti-cancer) agent and Sioshansi et al. teaches that in order to deliver both radiation and non-radiation treatments together it may be desirable to apply one more non-radioactive therapeutic agents. Therefore, when desiring to treat cancer it would have been obvious to one of ordinary skill in the art to incorporate an anti-neoplastic agent in combination with radionuclides, which is specifically designed to treat cancer. Further more, the selection of a specific drug is considered prima facie obvious depending on the desired condition/symptoms to be treated.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Lee and Sioshansi et al. utilize polyamino acids, nucleic acids, collagen or polypeptides. One of ordinary skill would have been motivated to utilize this material as the matrix as Lee teaches that these are suitable biocompatible materials. It would have been obvious to one of ordinary skill in the art to try any of the specifically taught biocompatible material as a person with ordinary skill has good reason to pursue known options within his or her technical grasp. **Note: MPEP 2141 [R-6]** *KSR International CO. v. Teleflex Inc.* 82 USPQ 2d 1385 (Supreme Court 2007).

Regarding claims 43-44, Lee teaches lengths and diameters of the cylinder that fall within those instantly claimed. Lee is silent as to the wall thickness or diameter of the hole. However, the shape of a ring delivery device has an outer diameter of 1.2 mm (0.05 in) and an inner diameter of 200 microns (0.2 mm and 0.008 inches), this corresponds to a wall thickness of 1 mm (0.04 inches). Therefore, based on this

teaching there is a reasonable expectation that the cylinder (in which the ends are ring shaped) would possess similar dimension to that taught of the ring shape. These ring dimensions fall within those instantly claimed. Furthermore, it would have been obvious to one of ordinary skill in the art to manipulate the size of the inner diameter and subsequently the wall thickness to additionally control the release rate of the drug. Therefore, when desiring a faster release, one of ordinary skill in the art would increase the inner diameter or when desiring a slower release one of ordinary skill in the art would decrease the inner diameter thereby manipulating the hole from which the therapeutic agent is capable of being released.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ABIGAIL FISHER whose telephone number is (571)270-3502. The examiner can normally be reached on M-Th 9am-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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AF

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Primary Examiner, Art Unit 1616